DR. BANDEEN-ROCHE: Yes, I would just -- I guess I would just voice my concern that the endothelial cell count data is such that at this point I don't feel like I can certify reasonable assurance of safety. Thus, I feel more of that data is necessary.

We've heard today that, you know, data that would suggest a leveling out or that would satisfy people's concerns really doesn't exist. I think maybe a few more years of data would be helpful. It might indicate a leveling out. It certainly would provide more individuals for the sorts of subset analysis that would feed into a grid.

DR. WEISS: So two to three year post-market.

DR. BANDEEN-ROCHE: Or pre-market. I'm just putting either one on the table.

DR. WEISS: Dr. McMahon.

DR. McMAHON: In the two areas in the post-market environment that I'm concerned with is the endothelial cell loss which I don't know if that's practical to track in a post-market study

surveillance. And the second is cataractogenesis which probably is. If it can be done for endothelial cell loss, yes, if that's not unduly burdensome.

I'll just step aside for one second and ask a question that pertains to the previous question in labeling, and that is in our discussion we talked about minimum refractive errors being changed from -5 to -9. Did that officially get into the labeling?

DR. WEISS: That's an excellent point. That's an excellent point. Let's just quickly go around with the post-market and then let's go back to the minimal refractive error. I thank you for bringing that to my attention.

Dr. Bradley, premarket, post-market, nothing?

DR. BRADLEY: Nothing.

DR. WEISS: Nothing. Dr. Macsai.

DR. MACSAI: My concerns have been addressed.

DR. WEISS: So you need neither premarket or post-market?

DR. MACSAI: No, by the previous comments.

DR. WEISS: Which one do you want? Do you want a premarket or a post-market or you do not?

DR. MACSAI: You mean I have to pick?

DR. WEISS: Do you want either of those or you are satisfied with not needing either of those?

DR. MACSAI: I want either. I want both.

DR. WEISS: Okay. So you would like either a premarket or a post-market.

Dr. Grimmett.

DR. GRIMMETT: I agree with Dr. Schein, affirmative post-market.

DR. WEISS: Post-market. Dr. Mathers.

DR. MATHERS: Post-market.

DR. WEISS: Post-market. Dr. Casey.

DR. CASEY: Post-market.

DR. WEISS: Post-market. Dr. Coleman.

DR. COLEMAN: Both.

DR. WEISS: Dr. Van Meter.

DR. VAN METER: I'm not sure I understand the benefit of additional specular cell counts the way we're doing them because I think they have muddied the water and I think more data of what we've got wouldn't

necessarily elucidate. It might be helpful to see maybe one more year's data on the cohort of patients that have already had the lens to be sure that nothing changes but I don't see a need for post-market surveillance.

DR. WEISS: Dr. Smith.

DR. SMITH: Both.

DR. WEISS: Dr. Huang.

DR. HUANG: Post-market.

DR. WEISS: Post-market. Just sort of for clarification, if you need further premarket data, that is, speaking that you would not be voting for approval, if you needed a post-market, that would be a potential condition that would get voted on separately from a main motion.

Dr. Rosenthal, correct me if I'm wrong.

DR. ROSENTHAL: You may vote for approval and still require additional pre-market analysis.

DR. WEISS: So do we need specification from those who wanted premarket as far as what they want?

DR. ROSENTHAL: No, I think we have a

sense of what they want.

DR. WEISS: You have a sense of what they want. Okay. And would that then be listed -- that would then be listed as a condition?

DR. ROSENTHAL: If it was approved.

DR. WEISS: If it was approved. If the main motion was approvable with conditions, that would be one of the conditions.

DR. ROSENTHAL: If not approvable, it would be one of the conditions that the company would have to fulfill to make it approvable.

DR. WEISS: Thank you for that clarification.

Now, we are going to go with one last and I think this is the last hopefully before the coffee break, is a minimal refractive error that you would consider for implantation of this lens.

Dr. Schein.

DR. SCHEIN: Nine.

DR. WEISS: Nine. Dr. Bandeen-Roche.

DR. BANDEEN-ROCHE: Defer.

DR. WEISS: Defer. Dr. McMahon.

DR. McMAHON: Nine.

DR. WEISS: Dr. Bradley.

DR. BRADLEY: I would select the mean suggestion of the panel.

DR. WEISS: There's one in every group. Dr. Macsai.

DR. MACSAI: Nine.

DR. WEISS: Dr. Grimmett.

DR. GRIMMETT: Ditto.

DR. WEISS: Dr. Mathers.

DR. MATHERS: Nine.

DR. WEISS: Dr. Casey.

DR. CASEY: Nine.

DR. WEISS: Dr. Coleman.

DR. COLEMAN: Nine.

DR. WEISS: Dr. Van Meter.

DR. VAN METER: Eight.

DR. WEISS: I stand corrected. There's two in every group.

Dr. Smith.

DR. SMITH: Nine.

DR. WEISS: And Dr. Huang.

DR. HUANG: Eight.

DR. WEISS: Let me just poll the panel. Does anyone here need a coffee break for 10 minutes or not? I don't see any affirmatives so we're forging on. Open public hearing session. Is there anyone who -- we have someone. Yes, please. If you could identify yourself. Seeing that many of my colleagues have just abandoned the ship, why don't we take that 10-minute coffee break and we'll be back here in exactly 10 minutes to hear your comments.

(Whereupon, at 4:36 p.m. off the record until 4:45 p.m.)

DR. WEISS: So if those of you who are here could take your seat we're going to be starting in just a few minutes. If you could make your comments brief, we are going to have the open public hearing session.

DR. JOHN: Ready?

DR. WEISS: Yes.

DR. JOHN: Hi. I'm Maurice John, an ophthalmologist from Louisville, Kentucky. I started implanting these lenses in October '98 and have done

over 200 of them. I would just like to make a few disjointed points.

First of all, there was some criticism because patients were done outside of the 20/40 range. I would point out that those are the patients who benefit the most from this and those are the people you should be improving.

They are 20/50, 20/60 from myopic degeneration because there is a huge chance that they are going to have an improvement in their best correctable vision. I have already had one patient who actually was able to get a driver's license, a 45-year-old business owner who went from 20/80 to 20/60. This is wonderful for those patients.

Also, the panel should be aware that right now refractive surgeons do not have many alternatives. I'm not a big proponent of clear lensectomy for myopes and I don't believe in it but that is being done and they are giving laser procedures done both PRK or ASA type procedures and LASIK most of which are being done with a blade with variable depths. This is a fabulous alternative compared to what is being done

out there and it's going to be done if they do not have some other alternative.

A prudent doctor, which I consider myself on most days, would certainly have your patients back every year for endothelial cell counts. I think that is going to address some of those concerns and that should probably be in your information that the FDA has put out encouraging patients to do that. Why wouldn't you do that?

One of the wisest things you've done today, and you may not be aware of it, but from my clinical experience was that you suggested that the anterior chamber depth be greater than 3.2 mm. I absolutely agree with you on that. This lens likes a little space and I think 3.3 and greater is very reasonable and appropriate and it's going to work well. It's going to cut down on some of these complications that you see. I'm quite sure of that.

As far as this lens in my six years and four months experience with it causing cataracts and retinal detachments, retinal detachments are the least of my concern for this lens that it's going to call

retinal detachment. I do not believe that for a second. As far as cataract, that's only the least of my concerns.

I would point out I do not consider cataract a benign complication of this lens and that's why I don't implant other lenses. There is a reason that 60 plus percent of the free market out there outside of the United States is using this lens when they have the options of using everything else that is out there.

Also, I think you are making a mistake in limiting this to 9 diopters. There are patients with incredibly thin corneas who are candidates for significant haze with a PRK procedure or cannot have a blade procedure or LASIK type procedure and this works well for them. Just because there was a little variability in the accuracy of this I don't think is a reason to exclude that. So my two cents worth. Thank you very much. Appreciate it.

DR. WEISS: Thank you.

Dr. Rosenthal, do you have any comments?

DR. ROSENTHAL: I do not.

DR. WEISS: Are there any closing comments by FDA? No? Then we will have any sponsor closing comments if they have for five minutes. Does the sponsor have closing comments? I guess so.

DR. STULTING: Thank you, Dr. Weiss, members of the panel. I appreciate your concerns about the safety and efficacy of the ARTISAN lens. In fact, I had many of these same concerns before I became an investigator in the study. Like Dr. Thompson, I was swayed by the international experience with the lens. I consider myself an average surgeon and I'll never forget the day that Rick McCarley coached me through my first case in 1998. With time I became comfortable with the surgical technique. After this personal experience I'm convinced that an effective training program can be constructed so that the lens can be safely implanted by an ophthalmologist with average surgical skill.

I've gotten to know my patients who have ARTISAN lenses and I can tell you that these are some of the most grateful patients in my practice. I'm here today because I truly believe this technology

should be available to physicians and patients in the United States.

As a resident I was taught that surgery was contraindicated in patients whose vision could be corrected with glasses and contact lenses. I now understand the disability that high myopes actually have.

My first ARTISAN implant was in a fire fighter who could not wear glasses or contact lenses safely in his work. Corneal surgery was contraindicated to him because of the degree of myopia and the corneal thickness. Every time I see him he thanks me for the difference I made in his life. This is not a new technology.

In fact, it is available virtually everywhere else in the world except the United States. Furthermore, surgeons who have a choice select the ARTISAN lens for implantation over other technologies. Dr. Budo who is with us today has freely chosen to implant the phakic lens for 18 years and the aphakic lens for 21 years. In my mind this speaks volumes about the lens.

If it caused a significant number of long-term complications it would be abandoned in a free market. If endothelial cell loss were a real problem with this lens, surely there would be at least one publication in the literature after implantation of 100,000 of these devices worldwide since 1986.

Surely Dr. Budo would tire of seeing complications from his implants. Indeed, this is the kind of post-market surveillance that impresses me. No surgical procedure is 100 percent safe. Balancing safety and efficacy I believe that this technology should be made available in this country to an appropriately selected patient population.

Age, endothelial cell counts, and refractive errors should be considered during the selection process. I believe that the comments provided today by the panel can give good guidance to the FDA and the sponsor so that this can be accomplished. I hope that the panel would choose to empower ophthalmologists in the United States to offer this surgical treatment to our patients particularly those who have no other option to correct their

refractive errors. Thank you.

DR. WEISS: Thank you, Dr. Stulting.

We will now have the voting options read by Sally Thornton.

MS. THORNTON: The medical device amendments to the Federal Food, Drug, and Cosmetic Act as amended by the Safe Medical Devices Act of 1990 allows the Food and Drug Administration to obtain a recommendation from an expert advisory panel on designated medical device premarket approval applications, or PMAs, that are filed with the Agency.

The PMA must stand on its own merits and your recommendation must be supported by safety and effectiveness data in the application or by applicable publicly available information. Safety is defined in the Act as reasonable assurance based on valid scientific evidence that the probable benefits to health under conditions on intended use outweigh any probable risks.

Effectiveness is defined as reasonable assurance that in a significant portion of the population the use of the device for its intended uses

and conditions of use when labeled will provide clinically significant results.

Your recommendation options for the vote are as follows: Approval given if there are no conditions attached. Approvable with conditions. The panel may recommend that the PMA be found approvable subject to specified conditions such as patient or physician labeling, labeling changes -- I'm sorry, such as physician or patient education, labeling changes, or a further analysis of existing data. Prior to voting all of the conditions should be discussed by the panel.

Not approvable. The panel may recommend that the PMA is not approvable if the data do not provide a reasonable assurance that the device is safe or if a reasonable assurance has not been given that the device is effective under the conditions of use prescribed, recommended, or suggested in the proposed labeling.

Following the voting the chair will ask each panel member to present a brief statement outlining the reasons for their vote. Thank you.

DR. WEISS: Thank you. Do I have a motion?

Dr. Schein.

DR. SCHEIN: I have a question.

DR. WEISS: Okay.

DR. SCHEIN: One of the conditions -- this description of approval with conditions that Ms. Thornton just read included approvable based on further analysis of existing data. Is that correct?

DR. WEISS: Yes.

DR. SCHEIN: I just need some education. Maybe others in the panel do as well. What if one requested further data, as many of us have done today, and then reviewed the data and based on the review decide that no, it's not approvable. In other words, you're in a situation now where you want to see more analysis of existing data but you don't know yet what it's actually going to look like.

DR. WEISS: Dr. Rosenthal.

DR. SCHEIN: I've never seen you speechless.

DR. ROSENTHAL: I've never had a question

like that before. We can handle analysis of existing data -- I mean, of data that is requested. If it is contrary to the recommendation of the panel, we will not go along with the recommendation of the panel.

For example, I'm just picking, if you have 100 patients in a study -- 200 patients and you saw 100 and there was a complication rate of two percent and you said, "Well, that may be okay but I would like to see another 50," we saw another 50 and it was 15 percent, we wouldn't accept that as a reasonable assurance of safety and efficacy, if I make myself clear.

DR. SCHEIN: Thanks.

DR. WEISS: Are you satisfied with that answer, Dr. Schein, or satisfied as one can be right now?

DR. SCHEIN: Yes.

DR. WEISS: Fine. Thank you.

Do I have a motion? Dr. Van Meter.

DR. VAN METER: I move that the ARTISAN lens be found approval with the conditions we have discussed which would include age, anterior chamber

depth, specular cell count, and degree of myopia specifications.

DR. WEISS: I think what we can do as a motion is approvable with conditions and then what we will --

DR. VAN METER: Then come up with the conditions.

DR. WEISS: Dr. Van Meter has a motion for approvable with conditions. Does anyone second that motion? Dr. Huang seconds that motion. Now what we will do is have someone propose each of the individual conditions. We will then --

MS. THORNTON: We do not vote at this point.

DR. WEISS: We do each of the individual conditions, we vote on each of the individual conditions, and then we vote on the main motion, i.e., Roberts Rules of Order, in my room at the time.

Does anyone have a condition?

DR. VAN METER: Can we just have Mike read them off since he's been scribing all these things?

DR. WEISS: Mike is getting some religion

here.

DR. VAN METER: My conditions will be most likely what is on Dr. Grimmett's list.

DR. WEISS: If we could have Dr. Grimmett so kindly read each of the conditions he has scribed.

MS. THORNTON: Yes, you can read the issues that you feel you want to enter as conditions and then we will vote on each condition individually. We will group -- we can have one condition as labeling just to clarify that. In that condition you can list the things that we talked about, or you want to talk about regarding labeling.

DR. WEISS: So basically if we are lucky enough that it was separated into labeling issues which should be at the end of the discussion, we can vote on those in one group. Then the nonlabeling issues, for example, the lowest level of myopia, the fact that there might be premarket or post-market studies that were requested, those things are separate conditions.

DR. GRIMMETT: The notes here obviously

are a tad schizophrenic here so I'll be jumping around. The first condition, limit the anterior chamber depth to those patients greater than 3.2 mm.

DR. WEISS: 3.2 and greater or greater than? Greater than 3.2. Do I have a second? Dr. Smith seconds. All those who agree with this, can you raise your hand?

MS. THORNTON: That's Dr. Huang, Dr. Smith, Dr. Van Meter, Dr. Coleman, Dr. Casey, Dr. Mathers, Dr. Grimmett, Dr. Macsai, Dr. Bradley, Dr. McMahon, Dr. Bandeen-Roche, and Schein in the affirmative. That's unanimous.

DR. WEISS: So that condition passes. Second condition. If it's too difficult to separate out labeling versus the other things, it might just be more expedient if we are out of order to vote on the separate labeling if it's too hard. If it's hard, we can just have you read off your list and we'll vote on each of them.

DR. GRIMMETT: I have to read them and see which is labeling. A lot of the first part of the discussion we had labeling mixed in. This one might

be a tough one but it's the conditions for the -- I guess the dioptic range is probably easy so let's do that. A condition is only approval for greater than 9 diopters of myopia.

PARTICIPANT: -9.0 to -20.0.

DR. GRIMMETT: -9.0 to -20.0, the full range.

DR. WEISS: Do I have a second? Dr. Mathers seconds. Those who would like the indications to read this is indicated for -9.0 to -20.0 diopters of myopia, can you please raise your hand in the affirmative.

MS. THORNTON: Dr. Huang, Smith, Van Meter, Coleman, Casey, Mathers, Macsai, McMahon, Dr. Schein.

DR. WEISS: Those who are against.

MS. THORNTON: Voting against.

DR. WEISS: And those who are abstaining.

MS. THORNTON: Dr. Bandeen-Roche, Dr. Bradley.

DR. GRIMMETT: Sorry. I'm trying to figure out what the next condition is. I'm on the

affirmative on that one.

MS. THORNTON: Okay. Dr. Grimmett voted affirmatively.

DR. WEISS: So we have two abstaining and the rest were affirmative so the motion passes.

Dr. Van Meter.

DR. VAN METER: By way of sponsor's request to consider a lower age group, might we vote again on 8? That would encompass another subset of patients.

DR. WEISS: Unfortunately that just passed.

DR. VAN METER: I think the question of yes or no on that was, you know 9, certainly --

DR. WEISS: You know what? You could propose -8.0 to -9.0. We have -9.0 to -20.0.

DR. VAN METER: I would like to propose -8.0 to -9.0.

DR. WEISS: Okay. Do we have a second? We have Dr. Huang seconding. For those of you who would like to expand the indications to include patients with -8.0 to -9.0 of myopia, can you raise

your hand in the affirmative?

MS. THORNTON: Dr. Van Meter, Dr. Huang.

DR. WEISS: Two affirmative. For those who would like to vote in the negative, can you raise your hand?

MS. THORNTON: Dr. Smith, Coleman, Mathers, Grimmett, Macsai, McMahon, and Schein.

DR. WEISS: And those who would like to abstain can you raise your hand?

MS. THORNTON: Dr. Casey, Dr. Bradley, and Dr. Bandeen-Roche.

DR. WEISS: So that motion does not pass.

Dr. Grimmett.

DR. GRIMMETT: Next condition had to do with Drs. Macsai and Mathers comments regarding determining or calculating backwards to determine the entry age which required specifying a target cell count at the time of death and assuming a two percent loss rate if I'm paraphrasing Dr. Mathers correctly.

DR. MATHERS: The two percent versus the lower quartile rate.

DR. WEISS: Are you including that in the

motion?

DR. GRIMMETT: Well, they're different. Lower quartile is different than assuming two percent.

DR. WEISS: So then if you can just make whatever motion that you would like to make and then we can have discussion.

DR. VAN METER: Dr. Rosenthal suggested we could leave this up to the Agency to do.

DR. WEISS: In terms of the quartile versus two percent? Ralph, what he just said that we can leave this up to Agency. What do you -- how specific do you want us to be in terms of this motion?

DR. ROSENTHAL: I'd like you to give us any guidance you feel reasonable but I don't want you to go cell by cell by age by age.

DR. WEISS: So can you state it in the most nebulous form possible? I think that's what we mean.

DR. GRIMMETT: I'll need some help from Dr. McMahon regarding the lower quartile recommendation to help me phrase that correctly.

DR. McMAHON: I think it would be easier

just to use the two percent because they are not going to be very different.

DR. GRIMMETT: Speak into your microphone.

DR. McMAHON: I'm sorry. We can use the two percent. They are probably not going to be very different.

DR. WEISS: Or you could say two percent of a quartile whatever the Agency deems more appropriate in this case to keep it broad. Why don't we say that? Would that be acceptable, Dr. McMahon?

DR. McMAHON: Sure.

DR. WEISS: Fine.

DR. McMAHON: The Agency will do it anyway.

DR. WEISS: So, Dr. Grimmett, can you restate that?

DR. VAN METER: Are we working backward from an average cell count?

DR. GRIMMETT: I think a threshold minimum cell count.

DR. WEISS: Which was stipulated by Dr. Schein as being 1,600.

DR. GRIMMETT: And by Dr. Mathers as 1,200.

DR. WEISS: So Dr. Mathers is just trying to help us out by making it even more general that the Agency will determine the age as well as the minimal cell count from which they will work backward from, as well as whether it will be quartile versus two percent cell loss in order to determine the minimum cell counts at various ages. That's the motion which Dr. Grimmett will repeat. Can you just say that's the motion and then you won't have to repeat that?

DR. GRIMMETT: Yeah, that's the motion.

DR. WEISS: Okay. That's the motion. Who seconds that's the motion?

DR. BANDEEN-ROCHE: Is there time to ask a question?

DR. WEISS: Yes. You can discuss it before we have a second. Do you want to amend it?

DR. BANDEEN-ROCHE: I just want to ask a question which is if the long-term endothelial cell count data leveled out magically and became evident that maybe other patients could benefit, then what

would happen? Would supplement come to expand?

DR. WEISS: Ralph.

DR. ROSENTHAL: Exactly. The company would submit a supplement requesting a change in the indications in labels.

DR. WEISS: So this is not written in stone. We are working on the basis of the data that we have.

DR. ROSENTHAL: Working on the basis of the data you have.

DR. WEISS: Fine. Do we have a second?

DR. McMAHON: Second.

DR. WEISS: Dr. McMahon seconds. All of those who want to vote in the affirmative of what will be labeled as that motion you can raise your hands.

MS. THORNTON: Drs. Huang, Smith, Van Meter, Coleman, Casey, Mathers, Grimmett, Macsai, Bradley, McMahon, Bandeen-Roche, and Schein. That's 12 votes. That's unanimous.

DR. BRADLEY: I think as said that motion was almost unintelligible but I do believe the FDA understands.

DR. WEISS: That's why we have transcripts.

DR. BRADLEY: In the transcript it's going to be nonsense.

DR. WEISS: Maybe more intelligible than some of these meetings.

Dr. Grimmett.

DR. GRIMMETT: It's my belief that the remainder of the comments are specific to labeling.

DR. WEISS: Great.

DR. GRIMMETT: There's one issue

DR. BRADLEY: The age?

DR. GRIMMETT: The age was going to be back-calculated.

DR. WEISS: Independently there was a discussion on an age cutoff. The majority of the panel members had no opinion and there were two panel members that wanted a lower-age cutoff at 30. I don't know if you feel this way anymore, Bill, who mentioned an age cutoff of 40.

You can put forward a motion for a lower-age cutoff if someone wants to regardless of what the

Agency finds. You can say, "Hey, I don't want it to be done in lower than this." If that's the motion you want to make, then that's the motion you'll present. That wasn't really totally determined in our discussion.

Does anyone want to make that motion that there should be a lower-age cutoff? Dr. Van Meter.

DR. VAN METER: I would move that the lower age be 30.

DR. WEISS: Is there anyone who seconds that motion.

DR. McMAHON: Second.

DR. WEISS: Dr. McMahon seconds. Can we have a vote on having the lower-age cutoff being 30? All of those who agree, can you raise your hand?

MS. THORNTON: In the affirmative Drs. Huang, Van Meter, Mathers, McMahon. That's four. Those against?

DR. WEISS: Those abstaining?

MS. THORNTON: Dr. Schein, Dr. Bandeen-Roche, Dr. Bradley, Dr. Grimmett, Dr. Casey, Dr. Coleman, and Dr. Smith.

DR. WEISS: That motion does not pass. Dr. Macsai also abstained.

MS. THORNTON: Sorry.

DR. WEISS: That motion did not pass.

Dr. Grimmett.

DR. GRIMMETT: Next condition, as Dr. Schein suggested, is a post-market surveillance study including the factors he listed which I believe include explantation, retinal detachment, cataract formation, etc., with a sample size calculated using proper statistical methods by the agency followed for two to three years.

DR. WEISS: Anyone second? Dr. Schein seconds. Can we have a vote? All those in the affirmative, raise your hand.

MS. THORNTON: Dr. Huang, Dr. Smith, Dr. Van Meter, Dr. Coleman, Casey, Mathers, Grimmett, Macsai, McMahon, Bandeen-Roche, and Schein in the affirmative.

DR. WEISS: That passes. Any negative votes?

MS. THORNTON: Dr. Bradley negative.

DR. WEISS: Any abstentions?

DR. GRIMMETT: Let me do this one first. There was a discussion regarding an issue that Dr. Casey brought up followed up by Dr. Macsai that the minority population was insufficiently studied, Dr. Macsai pointing out that there were sufficient patients with the suggestion to reanalyze the data on the existing minority patients out to some appropriate interval. What were you looking for, Dr. Macsai? To find what type of analysis?

DR. MACSAI: I was curious about the intraocular pressure and gonioscopic evaluation.

DR. GRIMMETT: Pigment dispersion?

DR. MACSAI: And pigment dispersion in those populations including actually those with brown irides.

DR. GRIMMETT: So the motion is -- the stated motion is -- they don't have gonioscopy.

DR. COLEMAN: Could we make it more general maybe to make it for premarket studies? For premarket studies including further evaluation of subjects that are minority and have darker irides for

gonioscopy and endothelial cell count follow-ups and intraocular pressure?

DR. WEISS: That could be the motion if you would like.

DR. COLEMAN: That would make it a bit more general. And also stratification of the data as elucidated by Dr. Roche and Schein. You wanted the data presented differently for premarket studies.

DR. WEISS: I think we're having -- what is being suggested right now by Dr. Coleman is an inclusive motion to include all the data that you would like through a premarket study. She's trying to be inclusive. That could be added. You can add to that right now while she does the motion.

DR. ROSENTHAL: Excuse me, Madam Chairman.

DR. WEISS: Dr. Rosenthal.

DR. ROSENTHAL: If you listen to Ms. Thornton's reading, it says that it's a reanalysis of the existing data. If you want additional patient data included in the analysis, then it can't be a condition of approval because the approval is based on the existing data but a reanalysis of the data is

acceptable.

If you said you want a company to provide us with information on the rate of pigmentary dispersion, rate of cataract formation, rate of chronic iritis and secondary glaucoma in the patients who have already been studied, that would be a condition of approval. If you said we want an additional 250 patients to come to three years, that cannot be a condition of approval. That is new data. I have the boss here, Nancy Pluhowski, who makes it absolutely clear that that's the way we have to go.

DR. WEISS: Dr. Schein.

DR. SCHEIN: Dr. Rosenthal, I think that actually clarifies my question that stumped us 15 minutes ago.

DR. ROSENTHAL: That I didn't clarify before.

DR. SCHEIN: So that if there is a desire to have two year data on a greater proportion than the current portion which we have today, you cannot approve based on that. You have to not approve and then come back another day.

DR. ROSENTHAL: That is correct.

DR. WEISS: So can we have a motion that would make sense as far as a condition which is --

DR. GRIMMETT: Reanalyze existing data for minority subset to include those patients with brown irides but that's the motion.

DR. WEISS: That's the motion. Do we have a second of that motion? Dr. Casey seconds that motion. Do we have discussion on that motion?

DR. GRIMMETT: Well, the discussion would be the things that were mentioned they are looking for don't exist. There are no gonioscopy and no one looked for pigment dispersion in the angle and those data don't exist.

DR. WEISS: Can we have a vote? All those in the affirmative raise your hand.

MS. THORNTON: The affirmative is Dr. Smith, Van Meter, Coleman, Casey, Mathers, Grimmett, Macsai, Bradley, McMahon, Bandeen-Roche, and Schein. That's 11. In the negative?

DR. WEISS: Abstentions? One abstention.

MS. THORNTON: Dr. Huang.

DR. WEISS: The motion passes. To make things easier perhaps, what we can have you do is just read the rest of the things you have written.

DR. GRIMMETT: I think they're all labeling.

DR. WEISS: Even if they are labeling.

DR. GRIMMETT: I think they're all labeling.

DR. WEISS: So if you could just read them out, call them labeling and if something is not, you can circle it and we'll go back to it. Right now we are going to be reading all the labeling conditions and we will vote on them in one group. Labeling items. Excuse me. The condition which is going to be labeling items.

DR. GRIMMETT: All right. There's a condition for the following labeling conditions -- items. Wrong word. Pardon me. Labeling items mentioned in the labeling is that trauma is a risk factor for intraocular lens dislocation. Example, boxing.

Dr. Macsai requested a report, or at least

a more comprehensive report on the safety data for Group E including those patients with custom IOLs, etc.

Perhaps through Dr. Schein there was a mention to more accurately report to the consumer the percentage and definition of the term adverse event.

DR. MACSAI: Can I make a motion?

DR. WEISS: Yes.

DR. MACSAI: I move that the data be basically reanalyzed to determine what the actual adverse event rate is.

DR. WEISS: It won't be a separate motion but what Dr. Grimmett can do is include that in his motion of labeling because we have a motion on the table now that he's reading.

DR. MACSAI: No, that's not a labeling issue. It's a condition.

DR. WEISS: Then don't do it now. Then hold it.

DR. GRIMMETT: In order to accurately report to the consumer the percentage implicit in that is to calculate it properly but we can hold that.

DR. WEISS: Keep on going.

DR. GRIMMETT: Dr. Macsai suggested properly or more completely stratifying the data by lens power for the whole group. That is the predictability plus or minus a half or plus or minus 1.

Dr. Mathers suggested that in the section that the FDA is going to calculate regarding the age and endothelial cutoffs that Dr. Gray's comment that the data suggest that 38 percent of subjects have a 50 percent reduction in 20 years. Was it 25 years? I thought it was 20. Okay. 38 percent of subjects have a 50 percent reduction in 25 years.

Dr. Bradley suggested that in the labeling include mention of the theory that when pupil size is greater than optic size there should be a problem with visual aberrations in spite of the fact that the study did not find that.

Dr. Macsai wanted in the labeling that the glare, starburst, and halo table, those patients that said preoperatively no and they converted to postoperatively yes be included in the labeling.

Anne Coleman had a long list of suggestions that she has accurately transcribed onto the labeling sheets themselves that I will just include as the Coleman suggestions because it's too long. I'm not sure I accurately transcribed it so if that is okay with everyone, I will include Dr. Coleman's glaucoma suggestions.

DR. WEISS: That's fine. In the patient information booklet on page 8 Dr. Grimmett has a written comment about indicating that the patient's visual acuity at distance will be improved as opposed to using the words that the visual acuity will be clear.

DR. GRIMMETT: On page 13 delete the statement that the safety and efficacy has not been established if, indeed, it's approved. The other comment is that in the labeling mentioned that the long-term risks to the endothelium has not been established. Also comment that the short-term cell count is decreasing.

DR. BRADLEY: Mike, I think I made that suggestion. I think the important thing is that the

patient understand the concern that we have about those reduced cell counts. That needs to be in the labeling.

DR. GRIMMETT: I have that a little bit lower. Dr. Bradley wanted in the labelling concerns about future risks and extrapolations and the vast uncertainty about the future and health of the endothelium and what that means both to the physician and patient. Additional labeling concern regarding future risk for retinal detachment, cataract formation.

Dr. Bradley added that there is a statement regarding magnification of facts when moving a myopic correction from the spectacle plane to the iris plane. Dr. Weiss wanted in the labeling to describe in the patient labeling what it means to the patient to have corneal edema and cataract surgery if that does develop. I may have stated this. Dr. Weiss wanted information regarding the occurrence of lens opacities in the future is unknown.

Dr. Macsai wanted the contrast sensitivity information clarified with a comment that the

spectacle use in the pre-op testing versus iris plane IOL testing does not indicate improved contrast sensitivity following the procedure.

Dr. Schein had some labeling recommendations. Please correct me if I don't accurately transmit them. There was an inference you were commenting about the total number of eyes in the study wasn't clear throughout the document that you wanted fixed in the labeling. Also I believe there was an inference that it was a three-year study that you believe wasn't accurate in the labeling. You want that better clarified.

DR. SCHEIN: You might just summarize it as improvement in clarification of study size, duration, and complication rates.

DR. GRIMMETT: Okay. Good. So stated. Thank you.

Dr. Schein suggested in the labeling to list the number of surgeries on a per-eye and per-person basis. Dr. Schein --

DR. SCHEIN: Adverse events.

DR. GRIMMETT: You want adverse event

reporting more complete in the labeling?

DR. SCHEIN: On a per-eye and per-patient basis.

DR. GRIMMETT: Okay. You want adverse event reporting on a per-eye and per-person basis. I think you stated that in the complication section you didn't see lens opacity listed? I think there was some clarification needed regarding the term complication and adverse events.

DR. SCHEIN: Correct.

DR. GRIMMETT: Okay. Dr. Schein suggested in the labeling regarding the cell loss data that there is a listing not just of the mean cell loss rate but the percentage of patients losing certain increments such as 10 percent of cells, 20 percent of cells at various time intervals.

Dr. Schein suggested the deletion of the reference to the FDA grid regarding anterior chamber IOLs, that is.

Dr. Such had four comments regarding the labeling. She pointed out an inconsistency that the lower age range in the study was 21 years old and not

18 as was suggested in the current labeling. She wanted a precaution regarding low-level lighting and activities. She wanted a rework of the glossary as the terms were inaccurate and not comprehensible to the lay person. That concludes the labeling comments that I have.

DR. WEISS: Thank you so much for that exhaustive list and for scribing throughout this. Do we have a second to that motion? Dr. Schein has seconded. I would like to have a vote on the motion of all the labeling conditions that have just been read. Those who would like to vote in the affirmative, can you raise your hand.

MS. THORNTON: Dr. Huang, Smith, Van Meter, Coleman, Casey, Mathers, Grimmett, Macsai, Bradley, McMahon, Bandeen-Roche, Schein. Unanimous vote of 12.

DR. WEISS: Are there any other motions -- any other conditions that anyone would like to raise? Dr. Schein.

DR. SCHEIN: I would like to raise the same issue as relevant to the labeling. That is, we

have a per-person clinically significant complication rate estimate for this procedure. If I went back having spent umpteen hours on this, I could not tell another doctor or patient what I actually thought the cumulative complication rate was based on existing data.

DR. WEISS: Do I have a second?

DR. BANDEEN-ROCHE: Second.

DR. WEISS: Dr. Bandeen-Roche. Do we have a vote? Any discussion on this? There is no discussion. Can we have a vote? Those in -- Dr. Macsai.

DR. MACSAI: I would like to make it clear that these are adverse events and adverse reactions because they are different things and we can't have all these definitions that are different all the time. I had the same problem as Dr. Schein. It was not discernible to me from the data the way it was presented to determine what is the risk to the individual of any of those.

DR. SCHEIN: I purposely used the word clinically significant event. It has to be

recalculated based on a reasonable consensus of which one of those things we consider clinically significant and which you would not.

DR. WEISS: I think the Agency probably has a sense of what you're looking for. With that, can we have a vote? The Agency does have a sense. Correct?

DR. ROSENTHAL: Yes.

DR. WEISS: Okay. Can we have a vote? All those in the affirmative, please raise your hand.

MS. THORNTON: Dr. Huang, Smith, Van Meter, Coleman, Casey, Mathers, Grimmett, Macsai, Bradley, McMahon, Bandeen-Roche, Schein. Unanimous, 12.

DR. WEISS: Any other conditions? Dr. Macsai.

DR. MACSAI: I would like the results of both safety and efficacy of Group E to be made available to the Agency for evaluation. It was not in the volumes I was given. Maybe it was in the Agency's but not in what I reviewed.

DR. WEISS: I thought Dr. Grimmett

mentioned that.

DR. MACSAI: As a labeling issue.

DR. WEISS: I thought he mentioned it as a labeling. Does anyone else have the same recollection?

DR. MACSAI: I mean as a condition of approval. I'm asking this as condition of approval. That's different.

DR. WEISS: So as a condition of approval you want -- so this is basically sort of going with Dr. Coleman's motion of preexisting data that has not been analyzed.

DR. MACSAI: Yes.

DR. WEISS: So this is similar question, same data but here is another thing that you want to be looked at. Can you just restate that motion and we'll just then have someone second it if they will and then we'll have a vote.

DR. MACSAI: Data on safety and efficacy for Group E should be analyzed and reviewed by the Agency.

DR. WEISS: Do I have a second?

DR. McMAHON: Second.

DR. WEISS: Dr. McMahon seconds. Do we have a vote? Can we have all those who agree raise your hand in the affirmative.

MS. THORNTON: Drs. Huang, Smith, Van Meter, Coleman, Casey, Mathers, Grimmett, Macsai, Bradley, McMahon, Bandeen-Roche, Schein. Unanimous for, 12.

DR. WEISS: Does anyone have any other conditions? If not, then --

DR. VAN METER: Ms. Chairman, we at one time discussed -- we discussed contact lens refraction for the high myope group. This need not be a requirement but I would like for it to be a suggestion in the physician pamphlet suggesting that a contact lens refraction be used to determine -- suggested but not requiring that the contact lens refraction be used to determine the power in the high myope say over 12.

DR. WEISS: Do I have a second? Dr. Huang. Any discussion? Dr. McMahon.

DR. McMAHON: Are their nomograms going to be modified from that since we're dealing with a

different refractive swing? I understand your point. The issue is is that a burdensome thing that is unreasonable?

DR. WEISS: Well, it's burdensome only if you have a requirement of the company to give you more data. This is more of a recommendation in labeling. Since there is no data on this, you can say it's possible that it will improve your accuracy but we have no data whether it will or not so you can't put that in there. It's possible it will improve your accuracy and it's not putting any burden on the company.

DR. BANDEEN-ROCHE: Could you please restate the motion?

DR. VAN METER: I would like to suggest that a contact lens refraction could be used to improve the accuracy of the IOL power prediction in higher myopes. I'm thinking 12 or 14 as a number beyond which it might be helpful.

DR. WEISS: And that is a labeling issue that was not mentioned and that would just be put in the physician's handbook that it might be helpful.

Anyone have a second? Dr. Huang. Can I have a vote? All of those who would like that to be put in the physician's handbook can you raise your hand?

MS. THORNTON: Voting for, Dr. Huang, Smith, Van Meter, Coleman, Casey, Grimmett, Macsai. That's it.

DR. WEISS: All those who would like to vote against?

MS. THORNTON: Dr. Schein is voting against and Dr. Mathers.

DR. WEISS: Any abstentions? That passes. Any other motions? Not motions, excuse me. Any other conditions? If there are no other conditions, then we will have a vote on the main motion. We have already voted on each of the conditions. I will remind you the main motion is a vote for approvable with conditions so that is what we will be voting on now. For those who would like to vote in the affirmative that PMA P030028 should be approved with conditions, can you please raise your hand?

MS. THORNTON: Voting for Drs. Huang, Van Meter, Casey, Mathers, Bradley, McMahon. One, two,

three, four, five, six.

DR. WEISS: Those who would like to vote against, can you raise your hand?

MS. THORNTON: Voting against, Drs. Smith, Coleman, Grimmett, Macsai, Bandeen-Roche, and Schein. That's six against. This is your day, Dr. Weiss.

DR. WEISS: I would say might think this is the privilege of the chair. In this position I would say it's the burden of the chair but I will cast my vote in the affirmative for approvable with conditions. So the PMA as P030028 has passed with approvable with conditions. I will have a polling of the panel votes.

Dr. Huang, if you could just give us the reason why you voted the way you did.

DR. HUANG: I feel this device offers a reasonable alternative for the high myope patient and has adequate safety and efficacy.

DR. WEISS: Dr. Smith.

DR. SMITH: I feel that based on the information available to me today and the data available, I was unable to estimate overall risk of

clinically significant complications on a per-person basis and had existing concerns about extended endothelial cell loss.

DR. WEISS: Dr. Van Meter.

DR. VAN METER: I voted approvable with conditions and actually made the motion. My thinking is that it is definitely effective. It is safe within a subset of populations who have no other alternatives and for whom the benefits outweigh the risks with appropriate labeling.

DR. WEISS: Dr. Casey. Dr. Coleman. Excuse me.

DR. COLEMAN: I voted against approvable with conditions because although I felt the device is effective, I did not have reasonable assurance that it was safe because I need additional data to be collected.

DR. WEISS: Dr. Casey.

DR. CASEY: There is no doubt that there's a need for this device. Myopes of -9 and above within corneas are not candidates for LASIK. Contact lens intolerance that I've seen in these patients. People

who develop ulcers need another option.

While the data may not have been conclusive, I think certainly the trend was that it probably is efficacious and probably is safe. I think that when you take all that into consideration with the world experience and the conditions that we made today, I gave my vote in favor with conditions.

DR. WEISS: Dr. Mathers.

DR. MATHERS: I voted for approval with conditions knowing that there are risks associated with endothelial cell loss and other problems associated with its use. But I think that it can be used wisely and reasonably safely within a confined population that have no other good alternatives and clinicians should have this product available to them which is available all over the world otherwise. We can do so safely and wisely if we guide them appropriately.

DR. WEISS: I voted for approval with conditions because it was obvious from the panel discussion that the data that we needed to determine things definitively would not be available and by

appropriate restrictions and cautions through monitoring a minimal endothelial cell count and corresponding with the patient's age I hope that we can protect the patient population from endothelial decompensation while giving them the benefit of this exciting technology.

Dr. Grimmett.

DR. GRIMMETT: I voted against the motion because I was unconvinced of a reasonable assurance of safety based solely upon the data presented in the FDA study. Dr. Gray mentioned that based upon the current endothelial cell data, 38 percent of patients have 50 percent reduction over a 20 to 25-year period, an inference that is worrisome and does not convince me that this procedure is safe. Given my opinion that the endothelial data does not provide a reasonable level of safety, I cannot allow a subset of patients no matter how stringent the entry criteria to undergo that risk for a cosmetic elective refractive surgical procedure.

DR. WEISS: Dr. Macsai.

DR. MACSAI: I voted no. After analysis

of the data presented by the sponsor, there remain real questions about the endothelial cell loss rate in patients that have the ARTISAN phakic IOL implanted. As a result, I feel the sponsors have not established a reasonable assurance of safety of this device.

DR. WEISS: Dr. Bradley.

DR. BRADLEY: I voted approvable with conditions. The device is clearly highly effective. It also clearly comes with some risks. The risk is small and as long as we can preselect or eliminate potential patients who have the higher risk and communicate to those who are going to have the procedure what risks they are taking, it seems approvable.

DR. WEISS: Dr. McMahon.

DR. McMAHON: I voted approvable with conditions on the basis that it is safe on the short-term basis and efficacious. There are significant concerns with regard to long-term safety but, however, the actions of the panel in terms of the conditions, I think, are sufficient to safeguard long-term problems if they develop.

DR. WEISS: Dr. Bandeen-Roche.

DR. BANDEEN-ROCHE: I voted against approval because to vote for approval would have required me to certify that I found the data certified a reasonable assurance of safety. Key aspects were sufficiently uncertain that I could not do this to within a reasonable assurance. In combination with the concerns of my clinical colleagues, neither could I find for above a threshold of risk benefit.

DR. WEISS: Dr. Schein.

DR. SCHEIN: I voted not to approve based on my analysis of the data that was currently available today which I thought a follow-up of just over 50 percent of the cohort of two years was not enough to make the determinations that we require.

In general, I believe in not having a patronizing approach in the sense that we dictate our own personal levels of safety on the public. On the other hand, that demands that we are able to tell the public very accurately what the risks are and then let them determine whether that risk is adequate. I didn't feel that we were there based on what I had

seen so far.

DR. WEISS: We are going to have comments from the industry rep. as well as the consumer rep.

MR. BALO: This was very interesting for me and very overwhelming because I usually don't know much about ophthalmology but I sure learned a hell of a lot today. That's for sure.

I really would like to say that the sponsor and the FDA really have worked well together over many, many years to put this device on the marketplace. I sort of agree with the comments that were made by Dr. McMahon and Dr. Mathers. I do think there is a place for this device.

I think consumers should have other choices besides the choices they have today. I think it's good that we can have open debate, that industry can present their data, and that we can come to a reasonable conclusion that provides another alternative therapy for our patients.

DR. WEISS: Ms. Such.

MS. SUCH: On behalf of the consumers I want to thank the panel for taking into consideration

all the different patient concerns in the labeling that you have all expressed all day long. Also thanks for the piece that I had put in on behalf of the consumers that you actually accepted it into the labeling as you always do. Thank you very much.

DR. WEISS: You're welcome.

Dr. Rosenthal.

DR. ROSENTHAL: I just want to echo Ms. Such's thank you. I thought this was a very thoughtfully discussed. You made your decisions based on intelligent underpinning of a thoughtful process of what the Agency is meant to do. I am particularly thankful to those of you who called attention to protocol issues and hope that we will be able to address them in the future submissions. Thank you very much.

DR. WEISS: Thank you, Dr. Rosenthal.

Are there any other comments by members of the panel? If not, we will have comments by Sally Thornton.

MS. THORNTON: I have a couple things I just wanted to go over. These are sort of

housekeeping things. Members of the panel got these forms at their place. Would you please fill those out and give them to AnnMarie Williams. She is over there by the door. She needs to get those back before you leave today.

Also, would you please be careful. Leave on the table only the things that you do not want for tomorrow. Please take with you anything that you will need for tomorrow's review, discussion, any notes you've made for tomorrow's issues because overnight all of this on the table will disappear. Please just don't make that mistake.

I thank you very much for your attention and your time today. It's been long. It seems like endothelial cell data always ends at 6:00.

DR. WEISS: I want to thank members of the panel, the FDA, and the sponsor and this meeting is adjourned.

(Whereupon, at 5:46 p.m. the meeting was adjourned.)